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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/198,779	11/24/1998	STEFAN A. BLEDIG	04983.0002US	2937

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EXAMINER
ZHOU, SHUBO

ART UNIT	PAPER NUMBER
1631	29

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/198,779	Applicant(s) BLEDIG ET AL.	
	Examiner Shubo "Joe" Zhou	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

Applicants are hereby notified that the finality of the application has been withdrawn. Applicant's amendment and request for reconsideration in Paper #26, filed on 1/16/03, is entered. Applicant's Appeal Brief is acknowledged. Arguments in response to the previous Office action in the brief have been fully considered. The following rejections and/or objections are either reiterated from the previous Office action(s) or newly added, and constitute the complete set presently being applied to the instant application. Rejections and/or objections not reiterated from previous Office action are hereby withdrawn.

Claims 1 and 13 are currently pending and under consideration.

Specification

The specification is objected to because of the following:

The disclosure is objected to also because it contains an embedded hyperlink and/or other form or browser-executable code. Such code is present in the specification at page 12 and elsewhere. Applicants are required to delete all the embedded hyperlink and/or other form of browser-executable code. See MPEP ' 608.01. This objection is reiterated from the previous Office action, mailed 3/13/02.

Appropriate correction is required.

Claim Rejections-35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 and 13 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

The rejections and other rejections which follow are based on the following analysis of claims 1 and 13:

The claims would reasonably be interpreted to mean either (1) that SEQ ID NO:1 encodes the entire enzyme of maize methionine adenosyltransferase or (2) that its entirety encodes a fragment of the enzyme, i.e. every part of SEQ ID NO:1 encodes a portion of the enzyme, or (3) that it contained a nucleotide sequence that encodes a fragment of the enzyme. See the diagram sketch in the Appendix of this Office action.

A search of SEQ ID NO:1 suggests that SEQ ID NO:1 is a hybrid sequence containing elements from a "cDNA encoding corn protein phosphatase 2A regulatory subunit A" and a "cDNA homologous to methionine adenosyltransferase." This assertion is based on the following:

SEQ ID NO:1 is a nucleic acid sequence of 235 nucleotides long. A search of nucleic acid databases indicates that the first 121 nucleotides of SEQ ID NO:1 has a perfect match with a fragment of the cDNA encoding corn protein phosphatase 2A regulatory subunit A. See the attached sequence alignment between SEQ ID NO:1 and the sequence of Geneseq accession number AAA48574. Further, nucleotides 38-103 of SEQ ID NO:1 had a similarity of 75.8% with a sequence of a cDNA encoding wheat protein phosphatase 2A regulatory subunit A. See the

attached sequence alignment between SEQ ID NO:1 and the sequence of Geneseq accession number AAA48576. Interestingly, and it is important to notice that the sequence search results indicate nothing to support that the first 121 nucleotides encodes the enzyme of maize methionine adenosyltransferase or even anything similar thereto. On the other hand, nucleotides 159-235 of SEQ ID NO:1 has a high similarity with cDNA sequences from maize, wheat and barley. See sequence alignments between SEQ ID NO:1 and the sequences of Geneseq accession Nos. AAC47744, AAX07185, and AAT99143, respectively. Again, the sequence search results indicate nothing to support that this portion of SEQ ID NO:1 encodes the enzyme of maize protein phosphatase 2A regulatory subunit A, which is apparently encoded by nucleotides 1-121 of SEQ ID NO:1.

It should be pointed out that nucleotides 122-158 are a stretch of unidentified "Ns". Clearly, the sequence of SEQ ID NO:1 is a hybrid sequence containing elements of two distinct enzymes: corn protein phosphatase 2A regulatory subunit A and methionine adenosyltransferase, connected by an unknown sequence.

Therefore, a prima facie case exists that SEQ ID NO:1 is neither the complete sequence of methionine adenosyltransferase or a fragment thereof. On this basis, the assertion that SEQ ID NO:1 encodes the entire maize methionine adenosyltransferase or the entirety encodes a fragment of the enzyme lacks factual basis.

The utility of claimed nucleic acid molecules comprising SEQ ID NO:1 must relate to what it is. The available facts indicate that it is unknown what the entirety of SEQ ID NO:1 encodes or represents and therefore no evidence exists that it has a specific, substantial and credible utility.

To the extent that SEQ ID NO:1 contains a fragment of methionine adenosyltransferase cDNA that encodes a portion of the enzyme, one is left with the question of what the specific and substantial utility of the claimed nucleic acids is. Applicants argue in the brief that even if the claimed nucleic acids does not encode the maize methionine adenosyltransferase as asserted, specification also asserts that the claimed nucleic acids can be used as hybridization probe to identify polymorphisms, and the polymorphisms have utility for breeding plants with altered phenotypes. See page 5, lines 4-12. This is not found persuasive because this utility is not deemed specific and substantial. Even if the claimed nucleic acids molecules could be used to identify polymorphisms, the specification fails to describe any specific polymorphisms that can be identified and that is specifically linked to any altered phenotypes in order to be used in plant breeding. Thus, one of ordinary skill in the art would have to perform further research to identify any specific polymorphisms, to determine any links between the polymorphisms and any phenotype alterations in order to use such polymorphisms in breeding plants.

The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, and 13 are rejected under 35 U.S.C. 112, first paragraph.

Specifically, since the claimed invention lacks a patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The rejections of claim 1 and 13 are reiterated from the Office actions mailed 10/02/01 and 8/27/02, respectively, and maintained for reasons of record.

Claims 1 and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)), the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation; (b) the amount of guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the predictability of the prior art; (g) the breadth of the claims; and (h) the relative skill in the art.

(a) In the instant case, the amount of experimentation required by the skilled artisan in order to practice of using the claimed polynucleotides would require an unpredictable amount of experimentation for the following reasons:

(b) Claims 1 and 13 are drawn to nucleic acids encoding a maize methionine adenosyltransferase or a fragment thereof, wherein the nucleic acids comprise the sequence of SEQ ID NO:1. However, the specification only discloses the nucleotide sequence of SEQ ID NO:1, which encodes a fragment of methionine adenosyltransferase as set forth above. However, SEQ ID NO:1 contains 1) 37 Ns in the middle of the sequence, which can be any nucleotides, and 2) a sequence in the 3' portion that likely encodes corn protein phosphatase 2A regulatory subunit A, as set forth above. As set forth above, the entire sequence of SEQ ID NO:1 appears to be a hybrid of phosphatase 2A regulatory subunit A and methionine adenosyltransferase. The

specification does not provide adequate guidance with respect to the active domain or functional motifs of methionine adenosyltransferase and the correlation of such regions with SEQ ID NO:1. There is no guidance in the specification teaching a skilled artisan to use a polypeptide containing a region of protein phosphatase 2A regulatory subunit A and a small fragment of methionine adenosyltransferase as a functional methionine adenosyltransferase, i.e. having its enzymatic activity.

(c) The instant application does not present any working examples wherein the claimed polynucleotide comprising, or essentially consisting of, SEQ ID NO:1 is used to make a polypeptide and use the polypeptide as an active methionine adenosyltransferase.

(d)-(f) The nature of the invention, a polynucleotide comprising SEQ ID NO:1 being used as encoding an active methionine adenosyltransferase is complex. The sequence of SEQ ID NO:1 is not known in the prior art, nor is a polypeptide containing a region of protein phosphatase 2A regulatory subunit A and a small fragment of methionine adenosyltransferase. Gomez-Gmez et al. (IDS document: Plant Molecular Biology, Vol. 30, pages 821-831, 1996) compare the sequences methionine adenosyltransferase from a number of different species including *Arabidopsis thaliana*, *Dianthus caryophyluus*, and *populus deltoides*. See page 826, Fig. 2. None of the methionine adenosyltransferase appears to contain the portion of protein phosphatase 2A regulatory subunit A as contained in SEQ ID NO:1. Clearly, the prior art is unpredictable with regards to the use as an active methionine adenosyltransferase of a mosaic polynucleotide containing a region encoding a maize protein phosphatase 2A regulatory subunit A and a small fragment of maize methionine adenosyltransferase.

(g)-(h) The claims to polynucleotides comprising SEQ ID NO:1 encoding a methionine adenosyltransferase or fragment thereof are broad because SEQ ID NO:1 only comprises a small fragment of methionine adenosyltransferase and because the series of Ns in the middle of the sequence can be any nucleotide and thus encoding any amino acids. The level of skill of those in the art who practice making and using a polynucleotide comprising SEQ ID NO:1 as a methionine adenosyltransferase is high.

The skilled practitioner would first turn to the instant specification for guidance in practice of using a polynucleotide comprising SEQ ID NO:1 as a methionine adenosyltransferase. However, the specification does not provide sufficient guidance of practicing using the polynucleotides as claimed. As such, the skilled practitioner would turn to the prior art for such guidance. However, the prior art does not teach the nucleotide sequence of SEQ ID NO:1, nor a polynucleotide containing a region encoding a maize protein phosphatase 2A regulatory subunit A and a small fragment of maize methionine adenosyltransferase. Finally, the practitioner would turn to trial and error experimentation for using the claimed polynucleotides as methionine adenosyltransferase without guidance from the specification or the prior art. Therefore, undue experimentation becomes the burden of the practitioner.

In summary, the instant specification does not describe the invention in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the claimed nucleic acids comprising, or consisting essentially of, SEQ ID NO:1 as a maize methionine adenosyltransferase.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

This rejection is reiterated from the previous Office action mailed 8/27/02 and maintained for reasons of record.

Applicants argue in the brief that since the specification discloses the sequence of SEQ ID NO:1, it thus establishes possession of the claimed invention by applicants. This is not found persuasive for the following reasons:

Claim 1 appears to be drawn to a genus of polynucleotide including any polynucleotides comprising the nucleotide sequence of SEQ ID NO:1 that encodes a maize methionine adenosyltransferase or fragment thereof. While SEQ ID NO:1 may encode a fragment of a maize methionine adenosyltransferase, it does not contain a complete open reading frame encoding the full length maize methionine adenosyltransferase. Further, there is substantial variability among the species encompassed by the scope of the claim because the genus encompasses a variety of species which are yet to be discovered, such as full-length cDNA encoding the full-length maize methionine adenosyltransferase.

A description of a genus may be achieved by means of a recitation of a representative number of species, falling within the scope of the genus, or by means of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly & Co., 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In the instant case, since the specification discloses only a

species: a fragment of methionine adenosyltransferase encoded by SEQ ID NO:1, and, as set forth above, SEQ ID NO:1 is a partial cDNA that does not include any open reading frame of which it would be a part, the disclosure of one species, i.e. SEQ ID NO:1, would not be a representative number of species of the claimed genus. Further, since the claimed genus encompasses species yet to be discovered, e.g. full-length cDNA, the disclosed structural feature, i.e. SEQ ID NO:1, does not "constitute a substantial portion" of the claimed genus. Therefore, the disclosure of SEQ ID NO:1 does not provide an adequate description of the claimed genus.

All factors considered, 1) partial structure of the DNAs that comprise SEQ ID NO:1, 2) the breadth of the claim as reading on genes yet to be discovered, and 3) the lack of correlation between the structure and the function of the enzyme encoded by the claimed nucleic acids; in view of the level of knowledge and skill in the art, one skill artisan in the art would not recognize from the disclosure that the applicant was in possession of the genus of polynucleotides encompassed by the scope of the claim.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to:
Shubo "Joe" Zhou, Ph.D., whose telephone number is (703) 605-1158. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst Tina Plunkett whose telephone number is 703)-305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

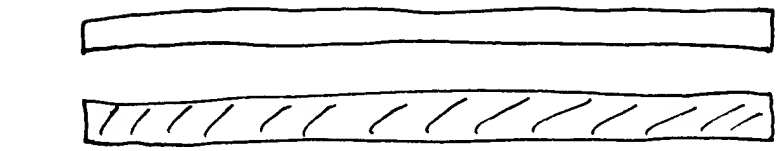
Shubo "Joe" Zhou, Ph.D.
Patent Examiner

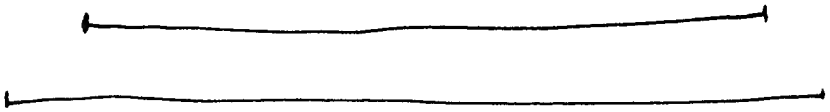
MICHAEL P. WOODWARD
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Appendix

claimed nucleic acid molecules

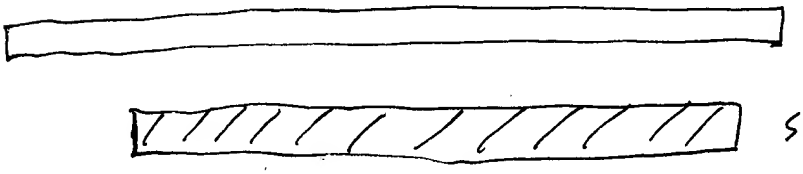
(1)

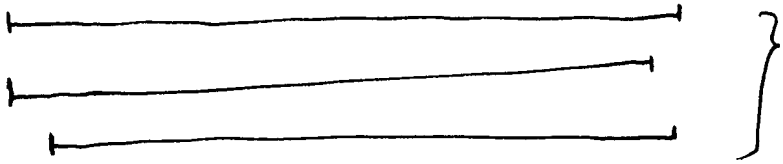




or

(2)





or

(3)